UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,751	08/17/2006	Francese Giancarlo	705152-2001	9535

23639 7590 09/08/2009

BINGHAM MCCUTCHEN LLP
Three Embarcadero Center
San Francisco, CA 94111-4067

EXAMINER	
RAO, SAVITHA M	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
09/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,751	GIANCARLO ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *005/04/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-43 and 47-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-43 and 47-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/21/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 28-43 and 47-57 are pending .

Receipt and consideration of Applicants' amended claim set and remarks/arguments filed on May 4th 2009 is acknowledged. Claims 28-43 are amended and claims 44-46 are cancelled and new claims 47-57 were added. The claims 26-43 and 47-57 are under consideration in the instant office action.

Applicants' arguments, filed 05/04/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 102(b)

This rejection is necessitated by the newly submitted claims filed on 05/04/2009.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 28-43 and 47-57 are rejected under 35 U.S.C. 102 (b) as being anticipated by Buchs et al. (US 5814635).is maintained for reasons of record restated below.

It is respectfully pointed out that claims 29-38 are product-by-process claims. As

per MPEP section 2113 (R-1) product by process claims. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113. Thus, because Buchs et al. teaches a product that is identical to what is instantly claimed, then the process limitations, while considered, are not patentably *limiting* to the claims because the prior art teaches an identical product and, therefore, the manner in which it was made fails to apparently result in a product different from that which is already known in the prior art.

Buchs et al. teaches a concentrated stable solution, especially an injection solution characterized in that it contains besides water either sodium-leucovorin or potassium-leucovorin or sodium-N(5)-methyl-5,6,7,8-tetrahydrofolic acid or potassium-N(5)-methyl-5,6,7,8-tetrahydrofolic acid (col.2, lines 15-19). Buchs et al. teaches that N(5)-Formyl-5,6,7,8-tetrahydrofolic acid, also named folinic acid, is used in the form of its calcium salt (calcium-leucovorin USP) as an agent in the cancer chemotherapy (col.1, lines 9-11). Buchs et al. teaches the method of preparation of the concentrated stable solution especially an injection solution where in Folinic acid or N(5)-methyl-5,6,7,8-tetrahydrofolic acid is suspended in degassed water at room temperature under an inert gas atmosphere. The water is acceptable for the preparation of injection solutions. An aqueous solution of sodium- or potassium-hydroxide, -hydrogen carbonate

or -carbonate is added in portions for a sufficient time until a clear solution is formed, which has the desired pH-value. The obtained solution is subjected to sterile filtration, and vials are filled with the resulting sterile solution under an inert gas atmosphere (col. 2, lines 20-32, patented claim 11).

Buchs et al. teaches that the preferred embodiments of his invention comprised more preferably from 2-6% weight of sodium-leucovorin or potassium-leucovorin or sodium-N(5)-methyl-5,6,7,8-tetrahydrofolic acid or potassium-N(5)-methyl-5,6,7,8-tetrahydrofolic acid (col.2, lines 33-39, patented claims 4- 5 and 13-15). Buchs et al. also teaches that the pH-value of the solution is more preferably 8.0 (col.2, line 40-41, patented claims 6-8 and 16) Buchs et al. additionally teaches that his invention also provides a concentrated, stable solution of the bases of folates, which contains neither a stabilizer nor complexing agents (col.2, lines 9-11). Note: It is a position of the examiner that the use of term “completing” in col.2, line 11 is a typo and is actually referring to the “complexing” agent, since the reference discloses that EDTA and similar complexing agents are not acceptable in an injection solution and it is the object of the invention to overcome that drawback in the prior art. Additionally the example of the preparation of the inventive solution does not include any stabilizing and complexing agent (page 2, line 65 to page 3, line 17).

Buchs et al. additionally teaches in example the preparation of inventive solution which comprises the following steps, 200.7 g of folinic acid with a water content of 10.2% by weight were suspended under stirring at room temperature in 2.5 liters of degassed, sterile water under a nitrogen atmosphere. Then was added drop by drop

under stirring a 10% aqueous sodium hydroxide solution until a clear solution has been formed, which had a pH-value of 8.0. The obtained clear solution was diluted to a volume of 3.6 liters by the addition of degassed, sterile water. This diluted solution was subjected to a sterile filtration (pore size: 0.2 micrometer). The obtained sterile filtrate was filled under a nitrogen atmosphere in vials. The vials were stored in a refrigerator at a temperature of 4.degree. C (page 2, line 65 to page 3, line 17).

Buchs et al. also teaches that the solution of his invention can be used in the preparation of a medicament for rescues/rescue agents after treatments with high doses of methotrexate or combined with 5-fluorouracil or used in the preparation of a medicament for the treatment of megaloblastic anemia and dihydropteridin reductase deficiency (col. 2, lines 56-62 and patented claims 17-20).

The instant claims recite a concentrated stable solution, **comprising** water and (6S)-sodium folinate or (6S)- potassium folinate. It is noted that the "comprising" language of the instant claims is open language that does not preclude the addition of other agents. Please see M.P.E.P. 2111.03. As such Buch's teachings of a concentrated stable solution, especially an injection solution characterized in that it contains besides water either sodium-leucovorin or potassium-leucovorin or sodium-N(5)-methyl-5,6,7,8-tetrahydrofolic acid or potassium-N(5)-methyl-5,6,7,8-tetrahydrofolic acid both of which are of the recemic form (R and S) still anticipates the instant claims, since the comprising language of the instant claims allows for the inclusion of the R form of the sodium or potassium folinate in the injection solution.

Accordingly claims 28-43 and 47-57 are anticipated by Buchs et al. et al.

Response to applicant's arguments filed on 05/04/2009:

Applicant traverses the above rejection with the following arguments:

a. The solution of Buchs et al. contains 50% of the inactive (6R) configuration of folinate.

b. The amorphous (6S)-folinic acid used for applicants claimed solutions has a stability comparable with that of (6RS)-folinic acid.

Applicant's traversal arguments for this rejection have been fully considered, but are not found to be persuasive.

In response to applicant's first argument that the solution of Buchs et al. contain a recemic mixture of folinate which includes 50% each of the R and S kind. As stated above in the new rejection, the **comprising language** of the instant claims allows for the inclusion of the R form of the sodium or potassium folinate in the injection solution as taught by Buchs et al. and therefore is anticipated by Buchs et al. .

In response to applicants argument that the amorphous (6S)-folinic acid in the applicants claimed solutions has a stability comparable with that of (6RS)-folinic acid., it is noted that the features upon which applicant relies (i.e.the stability) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant's statement

that the amorphous (6S)-folinic acid is especially suited for preparing concentrated stable solution is a mere allegation without any factual support.

Accordingly, the arguments set forth by the applicant are unpersuasive and the rejection is maintained.

Conclusion

Claims 28-43 and 47-57 are rejected. No claims are allowed

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 7.00 am to 4.00 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614